



The role of the transcription factors Bcl6 and Blimp-1 in intestinal dendritic cell subset specification

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genes involved in protein ubiquitination. De novo motif analysis (HOMER) revealed significant enrichment of IRF-associated transcriptional motifs (ISRE, EICE and AICE, $p < 1.6 \times 10^{-24}$) in the promoter binding sites, correlating with high level of expression of transcription factors from Interferon Regulatory Factors family.

Our analyses indicate chromatin state poises human LCs for efficient antigen presentation, indicating their adaptation to the specific requirements of the tissue compartment. These pre-determined LCs transcriptomic programmes can be rapidly initiated by signalling from the epidermis, leading to induction of efficient adaptive immune responses to the immunological challenge.

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MicroRNA-9 Promotes Dendritic Cell Activation Through Targeting PCGF6

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MicroRNAs (miRNA) are emerging as important regulators of immune function due to their fast action and their ability to regulate programs of gene expression. Dendritic cell (DC) responses to stimuli involves a rapid transition from steady-state an activated state, leading to numerous phenotypic changes underpinned by changes in gene expression. We have found that miRNA expression is dynamic following activation of DCs. Specifically, microRNA-9 (miR-9) expression is rapidly increased upon LPS stimulation, detectable as early as 10 min. One of the putative targets of miR-9 is Polycomb Group Factor 6 (PCGF6). Our lab has previously identified PCGF6 as a potent suppressor of DC activation, restraining DCs in the steady-state until it is rapidly downregulated following activation. We investigated whether miR-9 promotes DC activation through targeting of PCGF6.

We found that miR-9 directly targets the 3'UTR of PCGF6 in DCs. DCs overexpressing miR-9 showed an increased activation phenotype whereas DCs sequestering miR-9 via a miR-9 sponge showed blunted activation. Co-culture of miR-9 sequestering DCs with CD8+ or CD4+ T cells led to decreased T-cell activation and proliferation, whereas miR-9 overexpressing DCs promoted T cell activation. Mice immunized with miR-9-sponge expressing DCs following sub-cutaneous injection with B16-OVA melanoma cells displayed earlier onset of tumours and increased tumour volume compared to controls, demonstrating that miR-9 is necessary for proper DC function *in vivo*.

This work demonstrates that miR-9 promotes the activation and function of DCs, in part, through downregulating PCGF6, further adding to the growing evidence that miRNAs are involved in the regulation of immune responses.

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The role of the transcription factors Bcl6 and Blimp-1 in intestinal dendritic cell subset specification

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Dendritic cells (DCs) are the major antigen presenting cells of the immune system and play a pivotal role in immune activation versus tolerance in the small intestine (SI). DCs are classically divided into two major subsets: cDC1 (CD11b-CD103+) and cDC2 (CD11b+CD103+) DCs. cDC1 DCs are generally connected to antiviral and cancer immunity, whereas cDC2 DCs are highly effective in driving immune responses towards extracellular bacteria and parasites. Transcription factors (TFs) orchestrate the immune cell development and lineage specification. While cDC1 DCs critically depend on IRF8 expression, cDC2 DCs depend on the expression of IRF4. We have previously shown that the